Guidance for Industry

ANDAs: Stability Testing of Drug Substances and Products

DRAFT GUIDANCE

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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Contains Nonbinding Recommendations

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ANDAs: Stability Testing of Drug Substances and Products

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I. INTRODUCTION

This guidance recommends that abbreviated new drug applications (ANDAs) submitted pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act, and the drug master files (DMFs) that support ANDAs, follow the stability recommendations provided in International Conference on Harmonisation (ICH) stability guidances.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Over the past few years, the Office of Generic Drugs (OGD) has been receiving numerous inquiries about stability data requirements for ANDAs. Current published guidance from OGD consists of a 1995 industry letter which states OGD will accept ICH recommended long-term room temperature conditions for stability studies (i.e., 25±2°C, 60±5% RH). Although adequate in the context of other guidance existing at that time, this recommendation is no longer sufficient to serve as a basis for stability testing for ANDAs.

The following existing ICH guidances address stability for new drug substances and products:

1. Q1A (R2) Stability Testing of New Drug Substances and Products.

2. Q1B Photostability Testing of New Drug Substances and Products.

3. Q1C Stability Testing for New Dosage Forms.

[1] This guidance has been prepared by the Office of Generic Drugs, Office of Pharmaceutical Science in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

4. Q1D Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products.

5. Q1E Evaluation of Stability Data[2]

These will be referred to in the discussion that follows as ICH stability guidances.

III. DISCUSSION

Although the ICH stability guidances were developed by ICH to provide guidance on the information that should be provided in new drug applications to ensure the stability of new drug substances and drug products, we believe the recommendations should be applied to ANDAs as well.

When following the ICH stability recommendations, the applicant should:

1. Submit data from three pilot scale batches **or** two pilot batches and one small scale batch. If the size of the pilot does not follow ICH recommendations, the applicant should provide a justification.

2. At the time of submission, provide 6 months of data that include accelerated and long-term conditions. FDA recommends following ICH with respect to utilization of intermediate conditions to support shelf-life.

3. Use multiple lots of drug substance as appropriate.

4. Manufacture and package the drug product using principles that are representative of the commercial process.

5. Provide a fully packaged primary exhibit batch.

6. Use three batches when using bracketing and matrixing designs under ICH Q1D.

7. Provide statistical analysis of the data as appropriate, in accordance with ICH Q1E, Appendix A.

If you choose to deviate from the above recommendations, you should justify the approach you are taking.

[2] We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.